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ORIGINAL PAPER

Maja Steinlin · Katja Roellin · Gerhard Schroth

Long-term follow-up after stroke in childhood

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Abstract Over the last few years, the importance of paediatric stroke has become more and more evident; however, there is still little known about long-term neurological and especially neuropsychological outcome of these children. By retrospective chart review, questionnaire and clinical examination with structured interview, we analysed initial presentation, aetiology and long-term outcome of children suffering ischaemic childhood stroke between 1985 and 1999. A total of 20 children (13 boys) suffered acute arterial ischaemic events. Aetiology was detected in 14, and suspected in another five. Follow-up after 1–15 years (mean 7 years) was possible for 16 children; two had died and two were lost to follow-up. Only two were completely healthy, five suffered mild, six moderate, and three severe handicap. Eleven children presented with combined neurological and neuropsychological problems. Neurological problems were mild to moderate hemisyndrome in 11, dysphasia, epilepsy and other in six each. Mild to severe neuropsychological problems were detected in 13 children, school problems in eight, attention deficits in nine and behaviour problems in seven, increased fatigability and headache in six each. Recurrence was observed in three children, all due to progressive underlying disease. Outcome was most affected by the presence of combined cortical/subcortical and least affected by subcortical infarction. Epilepsy affected neuropsychological outcome. *Conclusion*: Although prognosis of paediatric stroke is better than for adult stroke, neurological and especially neuropsychological long-term problems significantly influence the lives of these children. Careful long-term follow-up to support these children in their school career and integration into professional life is necessary. Future studies should evaluate whether specific treatments during the acute episode could improve outcome for these children.

Keywords Behaviour · Neuropsychology · Outcome · Paediatric stroke

M. Steinlin (✉) · K. Roellin
Division of Paediatric Neurology,
University Children's Hospital,
Inselspital, 3010 Bern, Switzerland
E-mail: maja.steinlin@insel.ch
Tel.: +41-31-6329424
Fax: +41-31-6329500

G. Schroth
Department of Neuroradiology,
University Hospital Inselspital, Bern, Switzerland

Introduction

Stroke during childhood is a rare but terrifying disease, which differs significantly from adult stroke. Over the last few years, several papers have reinforced the importance of increased knowledge about stroke in children, especially regarding aetiology, outcome and also possible treatments to reduce morbidity, mortality and recurrence [5, 6, 8, 12, 13, 14, 16, 17, 18]. A broad spectrum of multiple risk factors leading to stroke in childhood [2, 4, 7, 9, 10, 13, 14, 15, 22, 23] clearly distinguishes from aetiologies in adult stroke. Considering these differences as well as the better capacity for recovery of the young brain, it becomes even more evident that outcome of children after stroke should be different from that of adults. Recent studies from the Netherlands [6], Canada [8] and Great Britain [12, 14] reveal that children after stroke not only face significant neurological, but also and especially neuropsychological and behaviour problems. Nevertheless, data on long-term follow-up of patients suffering stroke during childhood are very scarce. In a retrospective study, we analysed data of initial presentation and outcome of 20 patients who suffered stroke during childhood.

Patients and methods

Using a computer search, all children from the post-neonatal period up to 16 years, who suffered ischaemic stroke and who were treated at the University Children's Hospital in Bern were retrieved. Criteria for ischaemic stroke were: acute onset of focal neurological symptoms for at least 20 min with corresponding

ischaemic lesion on CT or MRI. Excluded were preterm children, children with neonatal or congenital infarctions, and children with diffuse asphyxia.

A retrospective chart review was performed, searching for information concerning family history, underlying disease, risk factors, clinical presentation, recurrence, treatment, follow-up and investigations for aetiology. All patients and parents received a questionnaire concerning actual health, problems in daily living, speech, social and school problems as well as their lifestyle satisfaction, related to the past history of stroke. Problems in daily living were evaluated by questions about age appropriate independency for activities as eating, dressing, brushing teeth, shopping, going to school, using public transportation etc. Speech problems were evaluated by function of expressive and comprehensive speech. School problems were evaluated by questions about need of special schooling, extra help and/or special therapies and for adult patients by degree of professional training and integration into professional life. Social problems were evaluated by questions about behaviour, integration into peer groups and family. Feeling of self-satisfaction was evaluated by questions about satisfaction within different areas as school, sports, friendships, general life as well as by a visual analogue grading system from 0 to 10 (mark on a line leading from 0 to 10). If possible, patients were seen for a structured history of their health status and a clinical examination. Clinical history, school performance and neuropsychological testing (available only for few patients) evaluated cognitive problems.

Neuroimaging (MRI, if not available CT) was reviewed for localisation and affected vascular territory. Localisation was divided into (1) cortical, subcortical white matter, (2) subcortical areas of basal ganglia, thalamus and internal capsule and (3) combination. The results were analysed for demographic data, clinical presentation, aetiology and long-term follow-up. Long-term follow-up was divided into neurological and neuropsychological outcome, with the following definitions: neurological symptoms: (1) mild: only detectable by neurological examination, (2) moderate: mild functional handicap (3) significant functional handicap or loss of function. Neuropsychological symptoms: (1) mild: detectable problems without significant handicap in daily living, (2) moderate: difficulties in school or professional life, but fully integrated in daily life (3) severe: significant problems with necessity for special schooling or special occupation. To judge independence we used the modified Rankin scale [24].

Statistical analysis to explore significance of localisation of infarction and of presence of epilepsy for prognosis of outcome was done by the two way classification of Chi squared.

Results

The records of 20 children (13 boys) were retrieved. All 20 suffered an arterial infarction and in one of these children arterial infarction was followed by a secondary sinus venous thrombosis. Age at manifestation was 6 months to 16.2 years (mean 7.3 years). In the 16 who returned the questionnaire, 14 were willing to undergo an additional follow-up examination. Two children had died due to their underlying disease (periarteritis nodosa and cardiac disorder respectively). Two children were lost to follow-up; from the limited chart review available, one of them had mild to moderate and the other a severe residual handicap. All together 16 children could be included into analyses for long-term follow-up.

Hemiparesis as the manifesting symptom was present in all 20 children. Accompanying facial paresis was present in 12 and aphasia/dysphasia in 10. Level of consciousness was reduced in six, with two children presenting in coma. Initial seizures were recorded for four and headaches prior to the insult in three children. A summary of proven and suspected aetiologies/risk factors is given in Table 1. Suspected aetiologies were considered in four children, where infarction followed within 3 weeks of a history of infection, and in the single child with an episode of marked sports activity and known history of polyglobaemia. For several children, a secondary risk factor could be detected in addition to a major aetiological risk factor. A summary of localisation and extension of infarction is given in Table 2.

Findings in the neurological follow-up are summarised in Table 3. Hemisyndrome was still present in 10/16 children, but all children showed at least a partial switch in hand dominance, if the dominant side was affected by the stroke. Problems of dysphasia were most pronounced in fluency and expressive language; two children showed isolated articulation problems resulting from tongue apraxia. Three children were known to have hemianopsia (cases 1, 7, 18), but only one manifested symptoms by bumping frequently into objects. Two children had facial paresis, but in neither was it a cosmetic or functional neurological problem. Another child suffered from tongue fasciculation and distal limb tremor.

Headache (6/18), was part of the initial presentation in one. In two children headache was a new complaint following the stroke, and in the other four headache changed characteristics after the stroke, becoming more severe and more frequent. Migraine was present in only two patients and in both the family history was positive for migraine.

Neuropsychological problems were present in 13/16. Children with stroke during school age showed significantly more academic problems afterwards, especially in the area of attention, concentration and processing time. For younger children, development was more affected. Three toddlers showed regression of development at the time of stroke and were afterwards delayed in their

Table 1 Aetiology of stroke

	Proven (*n*)	Suspected (*n*)	Secondary (*n*)
Vasculitis/infection	4	4	3
Periarteritis nodosa	1		
Focal vasulitis	2		
Para-infectious	1	4	3
Vasculopathy	4		
Moya Moya (-like)	3		
Fibromuscular dysplasia		1	
Cardiopathy	3		
Congenital cyanotic	2		
Acquired	1		
Coagulopathy	1	1	3
Protein S deficiency	1		
Polyglobulia/dehydration		1	
Stenosis/occlusion	2		
Uncertain	1		
Total (*n*)	15	5	6

Table 2 Summary of neuroimaging findings. (*Bil* bilateral, *L* left-sided, *MCA* middle cerebral artery, *PCA* posterior cerebral artery, *R* right-sided)

Patient	Size of infarction	Localisation				
		Vascular territory	Cortex/white matter	Basal ganglia	Internal capsule	Thalamus
1 [a]	+ +	MCA R	+	–	–	–
2	+ + +	MCA R	+	+	+	–
3	+ + +	MCA L	–	+	+	–
4	+ +	MCA L	–	+	+	–
5	+	PCA L	–	–	+	+
6	+	MCA R	+	–	–	–
7	+ + +	MCA L	+	–	–	+
8	+ +	MCA L	–	+	–	–
9 [a]	+ + +	MCA R	+	+ Bil	–	–
10	+ + +	MCA R	+	+	–	–
11	+	MCA R	–	+	–	–
12	+ + +	MCA L	+	+	+	–
13	+ +	MCA R	+	–	–	–
14	+ +	MCA R	–	+	–	–
15 [a]	+	MCA L	+	+	+	–
16	+ + +	MCA R	+	+	–	–
17	+ +	MCA L	–	+	–	–
18	+ + +	MCA L	+	–	–	–
19 [b]	+ + +	MCA L	+	–	–	–
20 [b]	+ + +	Multiple	+	+ Bil	–	+

[a]Neuroimaging not available for review, data from written reports
[b]Patient died

Table 3 Long-term follow-up neurological problems ($n = 18$); two lost to follow-up (patients 6 and 15)

Patient	Sex	Age at follow-up (years)	Years of follow-up	Hemisyndrome[a]	Diminished hand function[a]	Dysphasia[a]	Epilepsy[b]	Additional
1	M	12	10	+ +	+ +	+ + +	+ +	
2	F	15	4	+ +	+ + +	–	–	
3	M	10.5	1	+	+ +	+ +	–	
4	M	12.5	8	–	–	–	–	
5	F	17.5	6	–	–	–	–	Headache
7	M	7	2	+	+ +	+ + +	–	
8	M	7	2	–	–	–	–	
9	M	15	6.5	+	–	–	–	Headache/recurrence
10	F	14	9	+ +	+ +	–	–	Headache
11	F	8.5	5	–	–	–	+ +	Recurrence
12	M	23.5	9	+	+	+	–	Tremor
13	M	6.5	6	–	+	–	+	
14	M	12.5	6	–	–	+	+	Headache
16	M	14	12	+ +	+ + +	–	+ + +	
17	M	20	11.5	+	+	–	–	Headache
18	M	30.5	15	+	–	+ + +	+ + +	Headache
19[c]	F							
20[c]	M							Recurrence
Total (n)				10	9	6	6	

[a]Hemisyndrome, diminished hand function, dysphasia: + = mild (only detectable on neurological examination), + + = moderate (mild functional handicap), + + + = severe (significant functional handicap or loss of function)
[b]Epilepsy: + seizures in acute phase, + + seizure-free on follow-up but on medication, + + + recurrent seizures despite treatment
[c]Deceased

developmental milestones for sitting and walking. Compared with their siblings, all children showed marked problems in learning new activities and in achieving independence in daily living, affecting their school careers in many of them: five children required special schooling and three children had significant learning difficulties requiring educational assistance. The other eight children attended normal school, but many of them had additional academic problems, which were more pronounced than for their siblings. School difficulties were more obvious immediately after stroke and improved thereafter. Attention problems were reported in nine children, in one of them of severe and in four of moderate degree. Four of these five children attended special schools. For three children there were problems in hyperactivity. The parents of seven children reported increased sensitivity for changes in daily routine, which manifested mostly as behaviour problems such as emotional lability, temper tantrums and aggressive outbursts. In some of them, these problems prevented

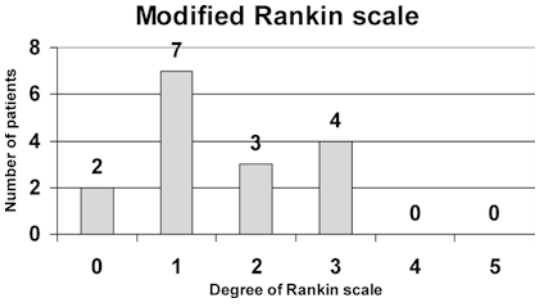

Fig. 1 Modified Rankin scale

participation at social events like birthday parties. Influence of neuropsychological problems was evident in using a modified Rankin scale (Fig. 1).

An interesting change in sleeping behaviour in 5/16 children was found on history, and although it became less problematic, it persisted for years. Compared with their siblings, these children fatigued faster and they needed more recreational time and sleep. These problems were sometimes a significant influence on family life.

Despite all these problems, contentment and self esteem for our patients were high; on a scale of 1–10, self-satisfaction ranged from 5 to 10 with a mean of 8.8. However, in discussion with patients and parents it became evident that neither patients nor parents thought it adequate to compare with healthy peers. Self esteem and contentment were judged by considering all the difficulties the children have had and still have due to their past stroke. The acute event was for most of them even after years still an alarmingly frightful time. It seems important to mention that for many children friendships became less, or even changed completely after stroke, indicating, that stroke had had a long-term effect on social life.

Recurrence was seen in 3/18 children. In all three of them the event was due to the underlying serious disease such as Moya Moya disease or periarteritis nodosa.

Prognostic analyses were limited due to retrospective study and small numbers of the group. A tendency for neurological problems to become more pronounced depending upon localisation (Fig. 2) was observed. Chi squared for localisation related neurological outcome was 11.85, for neuropsychological outcome 7.45. With 6 degrees of freedom, a level of significance of 0.05 was at 12.59, of 0.01 16.81 and 0.001 22.46. Patients with epilepsy demonstrated more neuropsychological problems than patients without (Fig. 3); however Chi squared of 3.556 ($P=0.05$ for 3 degrees of freedom 7.82), did not show significance.

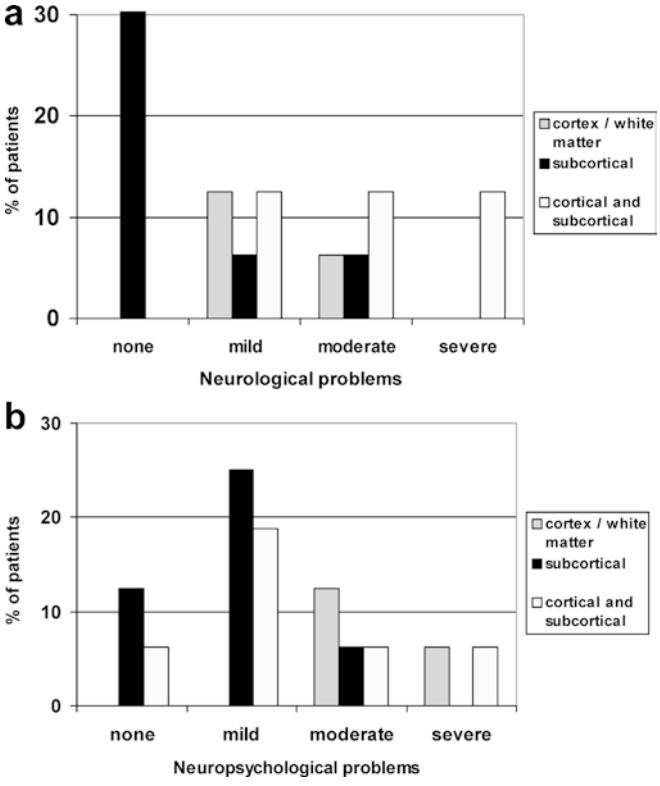

Fig. 2a, b Influence of localisation on prognosis

Discussion

Our demographic data largely correspond with previous studies [1, 6, 16, 19, 20, 25] with known preponderance of boys compared to girls. The reason for this imbalance is not known. In our study we could detect that coagulopathies were only present in boys. The male sex as a negative influence on coagulation was also discussed by DeVeber et al. [7]. Our demographic data have to be taken with caution, as these patients were retrieved in retrospect by computer analysis. There might also be a bias towards more severe cases, as the setting was a tertiary care university hospital.

The two peaks of increased frequency during preschool and teenage years could also be shown in our study. The reason for the peak during childhood is not completely understood. In this group, we found an increased frequency of para-infectious and cardiac causes. More frequent infections at this age allow for more frequent para-infectious complications. In contrary, for teenagers, we detected more frequent severe underlying problems such as fibromuscular dysplasia, periarteritis nodosa and leukaemia, in concordance with a study by Lanthier et al. [19]. The low frequency of sinus venous thrombosis in this study is probably related to our methods of data retrieval.

Long-term follow-up for children is better than for adults, where one third die, one third remain dependent and only one third can continue independent life. Most of our patients achieved an age-appropriate independency. Mortality in children is much lower and was in all three children based on a severe underlying disease and not a direct consequence of infarction.

An interesting observation is that self opinion and opinion by their parents is much better than clinical

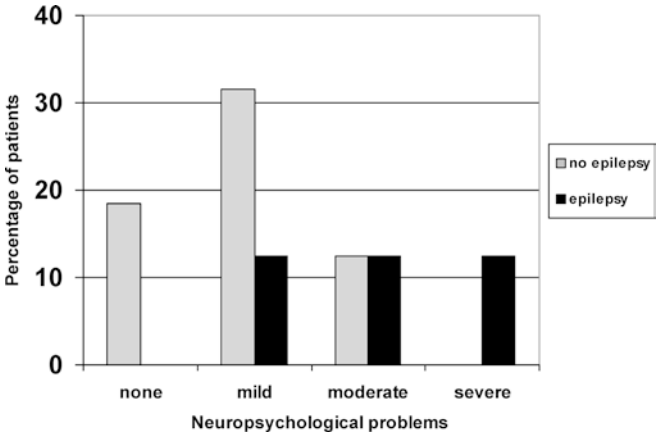

Fig. 3 Influence of epilepsy on neuropsychological problems

evaluation would suggest. This high satisfaction, which was also evident in the study of De Schryver et al. [6] might be explained by the drastic event of an acute episode of stroke. Even after years, there is still a high level of despondence in children and parents. This observation points to the importance of good psychological support during the acute episode.

A thorough clinical examination revealed that the majority of children are left with significant long-term problems. Full recovery could only be detected in 2 out of the 16 children followed long-term. This is in contrast to other studies which showed recovery rates of 25%–40% [1, 5, 6, 8, 19]. There is also discordance concerning frequency of neurological problems compared to neuropsychological problems, which in our study were represented about equally. With increasing insight into importance of neuropsychological handicap it seems likely that these problems have been underestimated in the past and were not sought. A similar study by Ganesan et al. [12] showed a similar recovery rate as in our study and also pointed out the importance of neuropsychological long-term sequelae. In general, neurological problems can be compensated for quite successfully, in contrast to neuropsychological problems which remain life-long handicaps.

Behaviour problems have been a frequent complaint in our study, with 44% of parents reporting behaviour problems most pronounced at home. This is in concordance with recent study of Ganesan et al. [12] with 37% of parents reporting behaviour problems and by De Schryver et al. [6] with 19% having behaviour changes at home and 29% with friends. These changes seem to be due to brain dysfunction and less due to frustration of the patients, as this would not correspond with their good self-esteem! We could not correlate behaviour problems with particular affected areas, which would point to the possibility that not only frontal lesions are prone to behaviour problems. Changes in sleep behaviour have not been reported in earlier studies. Increased fatigability was detected in 33% of our patients. These children had prolonged night sleep, but no problems in falling asleep or with nocturnal waking. These changes are probably not an effect of post-lesional dysfunction, but simply a consequence of increased daily burden.

We could not detect a relationship of migraine to stroke in childhood. However, there was an increased frequency of headache in our group of patients. The headache was either of new onset or changed quality after stroke. This points to the possibility that headache and stroke are interrelated. However, it remains uncertain whether an underlying disorder leads to stroke and headache or whether stroke itself influences headache.

Prognosis after stroke is difficult. Our study confirms the importance of the underlying disorder for prognosis and recurrence risk for children after stroke. Statistical analyses in this retrospective study of a small number of patients have to be taken with caution. Our findings that subcortical lesions have a tendency to better neurological prognosis than cortical lesions (chi squared just below the P level of 0.05) have also been described in other published studies [1, 3, 21]. However, there are some studies where the prognosis of subcortical strokes was worse compared with cortical strokes [9, 11], and De Veber et al. [8] could not detect any influence. Prognostic value of subcortical and cortical localisation of infarction remains uncertain. As in the study of Ganesan et al. [12], we could also detect children with small subcortical lesions but significant handicap. For neuropsychological outcome we could not detect significance for prognostic value of localisation of infarction. A further prognostic factor discussed is the presence of epilepsy on follow-up. Similar to the study of De Schryver et al. [6], we could show that children with epilepsy had more neuropsychological problems than children without. However, also these results did not show statistical significance. There was no influence of seizures on neurological outcome.

In conclusion, stroke in childhood is not only a terrifying event at the time of the acute episode, but remains a significant burden on long-term follow-up. Careful primary care and follow-up are mandatory. Stroke in childhood differs significantly from that in adults, with more variable risk factors and aetiology, and also in general a more favourable prognosis. Despite better prognosis, there remain significant long-term problems, most pronounced in neuropsychological function and behaviour. The lack of data in general and especially the missing prospective data concerning these problems show the necessity for such studies. Future studies should closely examine the effect of stroke on daily life and professional activities and standardised scales for such evaluations would be an advantage. Despite better outcome after stroke for children than for adults, the question whether more aggressive treatment (such as thrombolysis) during the acute episode might improve their outcome still awaits an answer.

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